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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,726	08/24/2001	Jing-Shan Hu	PF112P3D1C1	3533
22195	7590	06/28/2004	EXAMINER	
HUMAN GENOME SCIENCES INC INTELLECTUAL PROPERTY DEPT. 14200 SHADY GROVE ROAD ROCKVILLE, MD 20850			LANDSMAN, ROBERT S	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/935,726

Applicant(s)

HU ET AL.

Examiner

Robert Landsman

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-24, 32, 36, 39, 42-45, 47, 48, 55, 61, 67-70, 75-82 and 91-114 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 32, 36, 39, 42-45, 47, 48, 55, 61, 67-70, 75-82 and 94-114 is/are allowed.
- 6) ☒ Claim(s) 21-24 and 91-93 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Formal Matters

- A. The Amendment dated 5/7/04 has been entered into the record.
- B. Claims 1-90 were pending in the application. In the Amendment dated 5//704, Applicants canceled claims 1-20, 25-31, 33-35, 37, 38, 40, 41, 46, 49-54, 56-60, 62-66, 71-74 and 83 and new claims 91-114 have been added. Therefore, claims 21-24, 32, 36, 39, 42-45, 47, 48, 55, 61, 67-70, 75-82 and 91-114 are pending and are the subject of this Office Action.
- C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Double Patenting

- A. Claims 1-90 remain provisionally rejected under the judicially created doctrine of double patenting for the reasons already of record on pages 3-4 of the Office Action dated 2/17/04. The Examiner notes that Application No. 09/623,725 has been abandoned and that the claims in Application No. 10/127,551 are directed towards DNA, not towards proteins, as is the case for the present invention. With respect to the remaining applications, Applicants have agreed to file a Terminal Disclaimer in the instant case over any of the claims currently pending in any of the cited cases that issue or are allowed prior to allowance of the instant application.

3. Obviousness-Type Double Patenting

- A. The rejection of claims 1-90 as being rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over at least claims 1-15 of U.S. Patent No. 5,932,540 has been withdrawn in view of Applicants' submission of a Terminal Disclaimer.

4. Statutory Double Patenting

- A. The rejection of claims 8-14, 84 and 88-90 as being statutory double patenting over claims 5, 14 and 15 of US Patent 5,932,540 has been withdrawn in view of Applicants' cancellation of claims 11-14 in their entirety and of the offending subject matter from claims 84 and 88-90.

Art Unit: 1647

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 21-24 remain rejected and new claims 91-93 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 4-5 of the Office Action mailed 2/17/04. Applicants argue that, after entry of the current amendment, the pending claims will be directed towards fragments of the 350 amino acid sequence of the biologically active, truncated form of VEGF-2 that retain the conserved 8 cysteines and migrate on a gel at 21kDa. However, claims 21-24 and 91-93 only recite the positions of 4 cysteines. The remainder of Applicants' response is drawn towards arguing that the specification teaches that how the artisan would go about making and identifying functional fragments of VEGF (and cite Bowie et al. and Ostade et al.). However, the crux of the rejection hinges on the fact that only the VEGF proteins comprising the amino acid sequence containing all 8 of the cysteines is enabled. It is suggested that Applicants amend the claims to recite the sequence of the entire fragment which contains the 8 conserved cysteine residues. Applicants have not taught that changes in the protein fragment containing the 8 cysteines can be made without affecting the function of VEGF. The argument that methods of screening for compounds falling within the scope of the present invention may be known to the artisan and that some experimentation may be necessary to determine whether a polypeptide fragment retains the claimed activity does not necessarily make it undue is not persuasive since the breadth of the claims is, in fact, excessive without these specific teachings. The only requirement in claim 21 is that the fragment of this 350 residue protein must have 8 cysteines, of which only 4 are known. Even arguendo, the language '8 cysteines' is acceptable, this would allow for an alteration of the remaining 342 residues of VEGF. A cysteine is a cysteine. What provides its function is its tertiary conformation which is due in large part to the surrounding residues in the fragment. There is no requirement for any other residues in the claimed fragment. The fact that functional language is recited in the claims does not remedy this situation since only minimal guidance and working examples are provided in the specification of functional fragments, none of which only have 4 or 8 conserved cysteines of VEGF. It is believed by the Examiner that the entire VEGF fragment comprising these 8 residues is required for VEGF function, unless Applicants can demonstrate otherwise. It is believed that all pertinent arguments have been addressed.

Art Unit: 1647

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 21-24 remain rejected and new claims 91-93 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 5-6 of the Office Action mailed 2/17/04. Applicants argue that the instant specification provides a sufficient description of the claimed invention such that a skilled artisan would reasonably conclude that the inventors had possession of the invention at the time the application was filed and that the specification describes distinguishing attributes that are shared by members of the genus. For example, the specification describes a conserved functional motif of eight cysteine residues and the consensus sequence PXCXXXXRCXGCCN (SEQ ID NO:8), which is important in maintaining biological activity, such as endothelial cell proliferative activity (Specification, page 10, lines 17-27). Applicants also argue that the specification also provides guidance to the skilled practitioner other amino acid modifications, such as conservative amino acid substitutions (specification, Table 1, page 39) and phenotypically silent amino acid changes (Specification, pages 37- 38) that can be made and while maintaining the recited biological activity. Furthermore, at the time the instant specification was filed, it was common in the art to make changes to proteins through substitutions, deletions, insertions, and/or additions.

These arguments have been considered, but are not deemed persuasive for the reasons seen in the above rejection under 35 USC 112, first paragraph, scope of enablement. Claims 21-24 and 91-93 only recite the positions of 4 cysteines. However, the crux of the rejection hinges on the fact that only the VEGF proteins comprising the amino acid sequence containing all 8 of the cysteines is enabled. It is suggested that Applicants amend the claims to recite the sequence of the entire fragment which contains the 8 conserved cysteine residues. Applicants have not taught that changes in the protein fragment containing the 8 cysteines can be made without affecting the function of VEGF. The only requirement in claim 21 is that the fragment of this 350 residue protein must have 8 cysteines, of which only 4 are known. Even arguendo, the language '8 cysteines' is acceptable, this would allow for an alteration of the remaining 342 residues of VEGF. A cysteine is a cysteine. What provides its function is its tertiary conformation which is due in large part to the surrounding residues in the fragment. There is no requirement for any other residues in the claimed fragment. The fact that functional language is recited in the claims does not remedy this situation since only minimal written description is provided in the specification of functional fragments, none of which only have 4 or 8 conserved cysteines of VEGF. It is believed by the Examiner that the entire VEGF fragment comprising these 8 residues is required for VEGF function, unless Applicants can demonstrate otherwise. It is believed that all pertinent arguments have been addressed.

Art Unit: 1647

7. Conclusion

A. Claims 32, 36, 39, 42-45, 47, 48, 55, 61, 67-70, 75-82 and 94-114 are allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (571) 272-0887.

Official papers filed by fax should be directed to (703) 872-9306. Fax draft or informal communications with the examiner should be directed to (571) 273-0888.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-0700.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
June 21, 2004


ROBERT LANDSMAN
PATENT EXAMINER